Rec'd PCT/PTO 08 OCT 2004

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 23 JUL 2004
WIPO PCT

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
P118401PC-Zie		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP 03/03751	10.04.2003	10.04.2002
International Patent Classification (IPC) or both national classification and IPC		
C07D498/08		
Applicant		
UFZ-UMWELTFORSCHUNGSZENTRUM LEIPZIG-HALLE GMBH		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
07.11.2003	22.07.2004
Name and mailing address of the international preliminary examining authority:	Authorized Officer
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/03751

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-15 as originally filed

Claims, Numbers

1-18 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 18

   because:

   ☒ the said international application, or the said claims Nos. 18 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-18
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-18
Industrial applicability (IA)	Yes:	Claims	1-17
	No:	Claims	

2. Citations and explanations

   see separate sheet

III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 18 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).

V Reasoned statement under Art 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V.1 The present invention relates to N-(3-rifamycinyl)carbamates and their use for treating or preventing mycobacterial infections, especially tuberculosis.

V.2 Reference is made to the following documents:

D1: US-A-4 261 891, cited in the application
D2: US-A-4 124 585
D3: US-A-4 327 096
D4: US-A-4 876 258

V.3 Novelty

Document D1 discloses rifamycin derivatives substituted in the 3 position with an azacycloalkyl group (claim 1). Especially the 4-alkyl-1-piperazinyl derivatives have a pronounced anti-tuberculosis action (column 15, line 22-47).
Document D2 discloses rifamycin derivatives substituted in the 3 position with a group N=CH-X in which X is hetero(aryl) (claim 1). The compounds have antibiotic activity.
Document D3 discloses rifamycin derivatives substituted in the 3 position with a group N=CH-NR*R** in which R* and R** are alkyl or form a cyclic ring together with the nitrogen they are attached to (claim 1). The compounds have antibiotic activity (claim 11).
Document D4 discloses rifamycin derivatives substituted in the 3 position with 4-biphenylyl methyl-1-piperazinyl (claim 1). The compounds have antibiotic activity (claim 12).

A rifamycinyl derivative substituted in the 3 position with a carbamate group is disclosed in none of the documents. Claims 1-6 therefore fulfill the requirements of Art 33(2) PCT.

Claims 7-9 describe a method of preparing N-(3-rifamycinyl)carbamates and are novel by consequence.

Claims 10-15 describe the use of N-(3-rifamycinyl)carbamates and are novel by consequence.

Claims 16 and 17 describe a composition comprising N-(3-rifamycinyl)carbamates and are novel by consequence.

Claim 18 describes a method for preventing or treating a mycobacterial infection and/or a microbial infection using N-(3-rifamycinyl)carbamates and is novel by consequence.

V.4 Inventive step

Starting from documents D1-D4 the problem to be solved by the present application may be regarded as how to provide novel possibly improved N-(3-rifamycinyl) derivatives to be used as antimycobacterial agents. The solution of the applicant resides in providing of 3.-carbamate derivatives. As no comparative data with the 3-amino derivatives of the prior art are given (comparison has been made with rifampicine only, which does not contain a 3-amino side chain but a 4-methyl-1-piperainyliminomethyl group) inventive step can at present not be acknowledged (Art 33(3) PCT).

V.5 Industrial applicability

For the assessment of the present claim 18 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

V.6 Clarity

The scope of claim 1 is too broad (cf especially the term aryl). Examples are given only for R is (monohalogenated) alkyl and nitro phenyl. All the other structural variations seem to embrace possibilities not yet explored by the applicant and might comprise subject matter which does not solve the relevant technical problem.